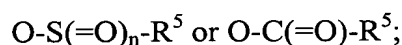
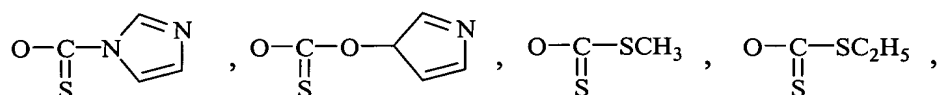


What is claimed is:

1. A process for the preparation of a 2'-deoxy- β -L-nucleoside comprising the steps of:

- a) selectively activating a 2'-hydroxyl of a β -L-nucleoside to form an activated nucleoside substituted at the 2'-position with a substituent selected from the group consisting of the following:



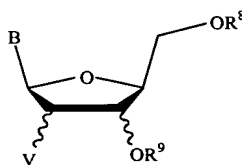
wherein n is 1 or 2 and R^5 is a hydrogen, an alkyl or aryl moiety; and

- b) reducing the product of step a with a reducing agent to form a 2'-deoxy-L-nucleoside.

2. The process of claim 1 wherein the reducing agent is tri-butyltin-hydride.

3. A process for the preparation of a 2'-deoxy-L-nucleoside comprising the steps of:

- a) preparing a 2'-halo-L-nucleoside of the following formula:



wherein B is a heterocyclic or heteroaromatic base,

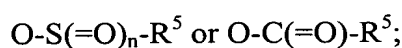
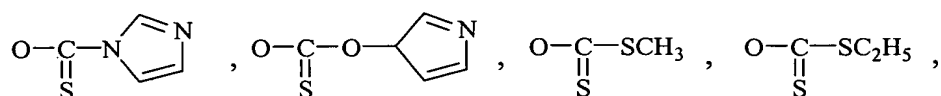
R^8 and R^9 are independently hydrogen or a suitable protecting group,

V is a halogen; and

- b) reducing the 2'-halo-L-nucleoside to a 2'-deoxy-L-nucleoside.

4. The process of claim 3 wherein the preparation of the 2'-halo-L-nucleoside comprises the steps of:

- a) selectively activating a 2'-hydroxyl of a L-nucleoside to form an activated nucleoside substituted at the 2'-position with a substituent selected from the group consisting of the following:

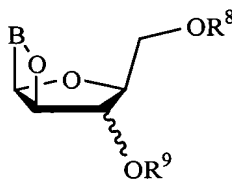


wherein n and R⁵ are previously defined; and

- b) substituting the 2'-moiety with a halide to give the 2'-halo-L-nucleoside.

5. The process of claim 3 wherein the synthesis of the 2'-halo-L-nucleoside further comprises the following steps:

- a) preparing from a suitably protected and activated L-nucleoside an anhydro-L-nucleoside of the following formula:

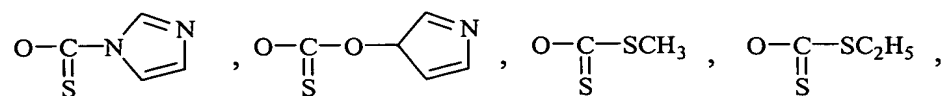


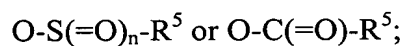
wherein B, R⁸ and R⁹ are previously defined; and

- b) substituting the 2'-moiety with a halide to give a 2'-halo-L-nucleoside.

6. The process of claim 5 wherein the synthesis of the anhydro-L-nucleoside further comprises the following steps:

- a) selectively activating a 2'-hydroxyl of a L-nucleoside to form an activated nucleoside substituted at the 2'-position with a substituent selected from the group consisting of the following:





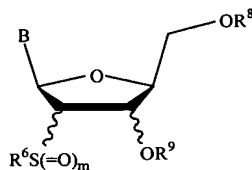
wherein n and R⁵ are previously defined; and

- b) intra-molecularly cyclizing the nucleoside with the heterocyclic or heteroaromatic base to form the anhydro-L-nucleoside.

7. The process of claim 3 wherein, the reduction of the 2'-halo-L-nucleoside comprises reducing via hydrogenolysis to obtain the 2'-deoxy-L-nucleoside.

8. A process for the preparation of a 2'-deoxy-L-nucleoside comprising the steps of:

- a) preparing from a suitably protected and activated L-nucleoside a 2'-S-substituted-L-nucleoside of the following formula:



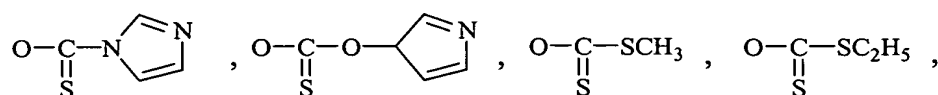
wherein B, R⁸ and R⁹ are previously defined,

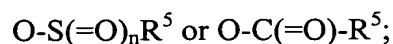
R⁶ is an alkyl or aryl, and m is 0, 1 or 2; and

- b) reducing the 2'-S-substituted-L-nucleoside to a 2'-deoxy-L-nucleoside.

9. The process of claim 8 wherein, the synthesis of the 2'-S-substituted-L-nucleoside further comprises the steps of:

- a) selectively activating a 2'-hydroxyl of a L-nucleoside to form an activated nucleoside substituted at the 2'-position with a substituent selected from the group consisting of the following:





wherein n and R⁵ are previously defined; and

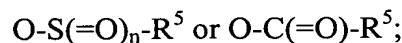
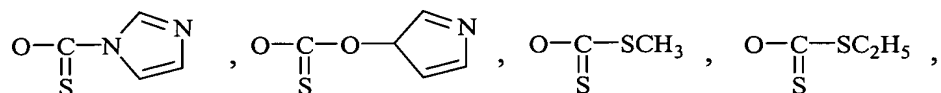
- b) substituting the 2'-moiety with a $\text{S(=O)}_m\text{R}^6$ or $\text{S(=O)}_m\text{R}^6$ equivalent to give the 2'-S-substituted-L-nucleoside.

5 10. The process of claim 9 wherein $\text{S(=O)}_m\text{R}^6$ is thioacylate or thiobenzoate.

11. The process of claim 9 wherein $\text{S(=O)}_m\text{R}^6$ is thioacetate.

12. The process of claim 8 wherein, the preparation of 2'-S-substituted-L-nucleoside further comprises the steps of:

- a) selectively activating a 2-hydroxyl of a L-furanose to form an activated furanose substituted at the 2'-position with a substituent selected from the group consisting of the following:



wherein n and R⁵ are previously defined;

- b) substituting the 2-moiety with $\text{S(=O)}_m\text{R}^6$ or $\text{S(=O)}_m\text{R}^6$ equivalent to obtain a 2-S-substituted-L-furanose; and

- c) coupling the appropriately activated 2-S-substituted-L-furanose with a heterocyclic or heteroaromatic base to form a 2'-S-substituted-L-nucleoside.

13. The process of claim 12 wherein $\text{S(=O)}_m\text{R}^6$ is thioacylate or thiobenzoate.

20 14. The process of claim 12 wherein $\text{S(=O)}_m\text{R}^6$ is thioacetate.

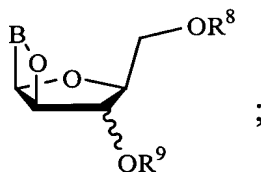
15. The process of claims 12 wherein the preparation of the suitably protected 2-hydroxyl-L-furanose does not comprise using mercury amalgam.

16. The process of claim 15 wherein the preparation of the suitably protected L-furanose is the synthesis of a suitably protected L-arabinose which further comprises the following steps:

- a) preparing a 5-O-silylated-L-arabinose;
- b) reacting the 5-O-silylated-L-arabinose with acetone and acid, optionally with a drying agent such as anhydrous copper sulfate, to obtain a 5-O-silylated-1,2-O-isopropylidene-L-arabinose;
- c) deprotection of the 5-O-silylated-1,2-O-isopropylidene-L-arabinose at the 5-position using fluoride ion to obtain a 1,2-O-isopropylidene-L-arabinose;
- d) protecting the 4 and 5 position of 1,2-O-isopropylidene-L-arabinose to obtain a 1,2-O-isopropylidene-4-O-protected-5-O-protected'-L-arabinose; and
- e) reaction of 1,2-O-isopropylidene-4-O-protected-5-O-protected'-L-arabinose with an alcohol to obtain a 1-O-protected''-4-O-protected-5-O-protected'-L-arabinose with a free 2'-hydroxyl.

17. The process of claim 8 wherein the preparation of 2'-S-substituted-L-nucleoside further comprises the following steps:

- a) preparing from a suitably protected and activated L-nucleoside an anhydro-L-nucleoside of the following formula:

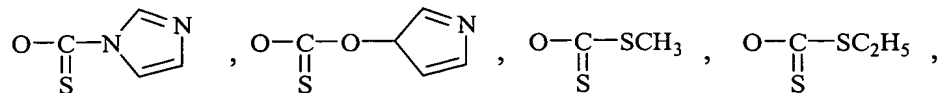


wherein B, R^8 and R^9 are previously defined; and

- b) substituting the 2'-moiety with $\text{S}(=\text{O})_m R^6$ or $\text{S}(=\text{O})_m R^6$ equivalent to obtain a 2'-S-substituted-L-nucleosides.

18. The process of claim 17 wherein the preparation of the anhydro-L-nucleoside further comprises the following steps:

- a) selectively activating a 2'-hydroxyl of a L-nucleoside to form an activated nucleoside substituted at the 2'-position with a substituent selected from the group consisting of the following:



5 $\text{O}-\text{S}(=\text{O})_n-\text{R}^5$ or $\text{O}-\text{C}(=\text{O})-\text{R}^5$;

wherein n and R^5 are previously defined; and

- b) intra-molecular cyclizing of the nucleoside with the heterocyclic or heteroaromatic base to form the anhydro-L-nucleoside.

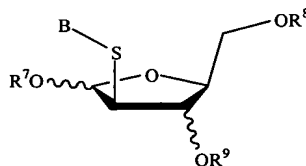
19. The process of claim 17 wherein $\text{S}(=\text{O})_m\text{R}^6$ is thioacylate or thiobenzoate.

10 20. The process of claim 17 wherein $\text{S}(=\text{O})_m\text{R}^6$ is thioacetate.

21. The process of claim 8 wherein, the reduction of the cyclonucleoside comprises the step of reducing via desulfurization with Raney Nickel to obtain a 2'-deoxy-L-nucleoside.

22. A process for the preparation of a 2'-deoxy-L-nucleoside comprising the following steps:

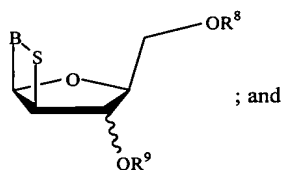
- a) preparing from a suitably protected and activated L-furanose a 2-S-substituted-2-deoxy-L-furanose of the following formula:



wherein B, R^8 and R^9 are previously defined;

R^7 is a suitable protecting group;

- b) cyclizing the 2-S-substituted-2-deoxy-L-furanose to form a cyclonucleoside of the following formula:



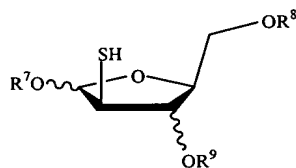
- c) reducing the cyclonucleoside to a 2'-deoxy-L-nucleoside.

23. The process of claim 22 wherein the preparation of the 2-S-substituted-2-deoxy-L-furanose comprises the following step:

- a) reacting an appropriately protected and activated L-furanose with a thio-heterocyclic or thio-heteroaromatic base.

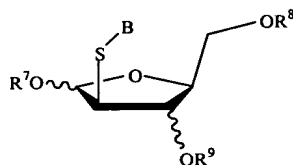
24. The process of claim 22 wherein the preparation of the 2-S-substituted-2-deoxy-L-furanose further comprises the following steps:

- a) preparing from a suitably protected and activated L-furanose a 2-thiol-2-deoxy-L-furanose of the following formula:



wherein B, R⁷, R⁸ and R⁹ are previously defined; and

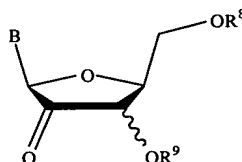
- b) coupling the 2-thiol-2-deoxy-L-furanose with a halo-heterocyclic or halo-heteroaromatic base to form a 2-S-substituted-2-deoxy-L-furanose of the following formula:



25. The process of claim 22 wherein, the reduction of the cyclonucleoside comprises the step of reducing via desulfurization with Raney Nickel to obtain the 2'-deoxy-L-nucleoside.

26. A process for the preparation of a 2'-deoxy-L-nucleoside comprising the steps of:

- a) preparing from a suitably protected and activated L-nucleoside a 2'-carbonyl-L-nucleoside of the following formula:



wherein B, R⁸ and R⁹ are previously defined; and

- b) reducing the 2'-carbonyl-L-nucleoside to a 2'-deoxy-nucleoside.

27. The process of claim 26 wherein, the reduction of the 2'-carbonyl-L-nucleoside comprises using hydrazine hydrate and hydroxide as the reducing agent.

28. The process of claim 26 wherein, the reduction of the 2'-carbonyl-L-nucleoside comprises the step of using tosylhydrazine followed by a borane or borohydride and optionally with an acetate as the reducing agent.

29. The process of claim 28 wherein the borane is catechol borane reacted with sodium acetate.

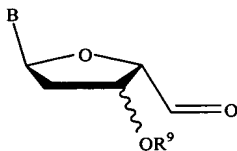
30. The process of claim 28 wherein the borohydride is sodium borohydride.

31. The process of claim 28 wherein the borohydride is NaBH₃CN.

32. A process for the preparation of a 2'-deoxy-L-nucleoside comprising the steps of:

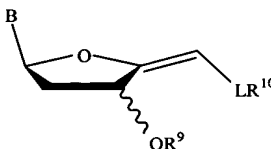
- a) preparing a suitably protected 2'-deoxy- α -D-nucleoside;

- b) oxidizing the 2'-deoxy- α -D-nucleoside to give an aldehyde of the following formula:



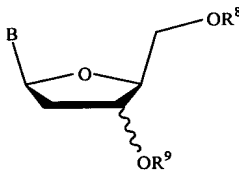
wherein B and R⁹ are previously defined;

- 5 c) converting the aldehyde to an enolacetate or enamine of the following formula:



wherein L is O or N; R¹⁰ is -C(=O)R¹¹ if L is O or R¹¹R¹² if L is N; and R¹¹ and R¹² are independently an alkyl or aryl group;

- 10 d) hydrogenating the enolactate or enamine to obtain a 2'-deoxy- β -L-nucleoside of the following formula:



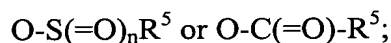
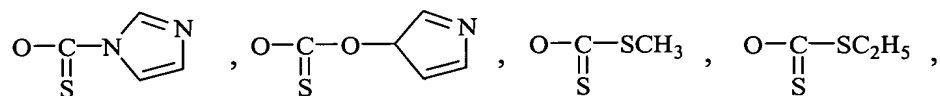
wherein B, R⁸ and R⁹ are previously defined; and

- e) optionally epimerizing the 3' position.

- 15 33. The process of claim 32 wherein the preparation of the 2'-deoxy- α -D-nucleoside further comprises epimerizing a corresponding, optionally protected, 2'-deoxy- β -D-nucleoside.

34. The process of claim 32 wherein the preparation of the 2'-deoxy- α -D-nucleoside further comprises the following steps:

- a) selectively activating a 2'-hydroxyl of a α -D-nucleoside to form an activated nucleoside substituted at the 2'-position with a substituent selected from the group consisting of the following:



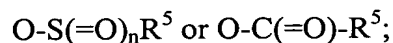
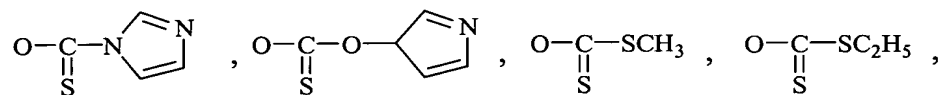
wherein n and R^5 are previously defined; and

- b) reducing the 2'-moiety with a hydride to give the 2'-deoxy- α -D-nucleoside.

35. The process of claim 34 wherein the hydride is generated from tri-butyltinhydride.

36. The process of claim 32 wherein the preparation of the 2'-deoxy- α -D-nucleoside further comprises the steps of:

- a) selectively activating a 2'-hydroxyl of a α -D-nucleoside to form an activated nucleoside substituted at the 2'-position with a substituent selected from the group consisting of the following:



wherein n and R^5 are previously defined;

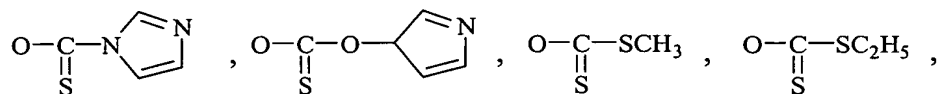
- b) substituting the 2'-moiety with a halide to give a 2'-halo- α -D-nucleoside; and

- c) reducing the 2'-halo-nucleoside to give the 2'-deoxy- α -D-nucleoside.

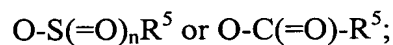
37. The process of claim 36 wherein the reduction is accomplished via hydrogenolysis.

38. The process of claim 32 wherein the preparation of the 2'-deoxy- α -D-nucleoside further comprises the following steps:

- a) selectively activating a 2'-hydroxyl of a α -D-nucleoside to form an activated nucleoside substituted at the 2'-position with a substituent selected from the group consisting of the following:



5



wherein n and R^5 are previously defined;

- b) substituting the 2'-moiety with a $\text{S}(=\text{O})_m\text{R}^6$ or $\text{S}(=\text{O})_m\text{R}^6$ equivalent, where R^6 is an alkyl or aryl moiety, to give a 2'-S-substituted- α -D-nucleoside; and

- c) reducing the 2'-S-substituted- α -D-nucleoside to a 2'-deoxy- α -D-nucleoside.

10

39. The process of claim 38 wherein $\text{S}(=\text{O})_m\text{R}^6$ is thioacylate or thiobenzoate.

40. The process of claim 38 wherein $\text{S}(=\text{O})_m\text{R}^6$ is thioacetate.

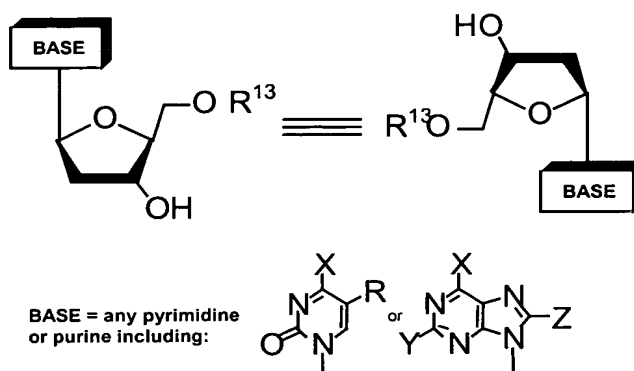
41. The process of claim 38 wherein the reduction is accomplished via desulfurization using Raney nickel to obtain the 2'-deoxy- α -D-nucleoside.

15

42. A process for the preparation of a 2'-deoxy-L-nucleoside comprising epimerizing the C-4' position of a pyrimidine α -L-nucleoside.

43. A process for the preparation of a 2'-deoxy-L-nucleoside containing a purine comprising base exchange with a pyrimidine β -L-nucleoside with a purine.

44. The process of claim 1, 3 or 8 wherein the preparation of a compound of the following formula (A):



(A)

5 wherein

X and Y are independently H, OH, OR, SH, SR¹, NH₂, NHR¹ or NR¹R²;

Z is hydrogen, halogen, CN or NH₂;

R is hydrogen, lower alkyl, aralkyl, halogen, NO₂, NH₂, NHR³, NR³R⁴, OH, OR³, SH, SR³, CN, CONH₂, CSNH₂, CO₂H, CO₂R³, CH₂CO₂H, CH₂CO₂R³, CH=CHR³, CH₂CH=CHR³ or C≡CR³;

R¹, R², R³ and R⁴ are independently a lower alkyl, e.g., methyl, ethyl, propyl, butyl, and alkyl possessing 6 or less carbons, in cyclic, branched or straight chains, unsubstituted or substituted wherein the alkyl bears one, two, or more substituents, including but not limited to, amino, carboxyl, hydroxy and phenyl;

R¹³ is hydrogen, alkyl, acyl, phosphate (monophosphate, diphosphate, triphosphate, or stabilized phosphate) or silyl; and

further comprising condensing 2-O-acetyl-1,3,5-tri-O-benzoyl-β-L-ribofuranose with a purine or pyrimidine base, followed by selective halogenation or thiocarbonylation at the 2'-OH group and subsequent reduction.

45. The process of claim 8 wherein the preparation of the compound of the above formula (A) further comprises converting L-ribose to a 2-deoxy-2-S-acetyl-2-thio-L-ribose

derivative which is then condensed with a purine or pyrimidine base to obtain only the desired β -nucleoside followed by desulfurization.

46. The process of claim 22 wherein the preparation of the compound of the above formula (A) further comprises synthesizing a 2-thiol-L-arabinose derivative from L-ribose, then
5 linking a purine or pyrimidine base to the sulfur, forming a glycosyl C-N bond between the sugar and the base to obtain only the desired β -anomer, and reducing by desulfurization.

47. The process of claim 1, 3 or 8 wherein the preparation of the compound of the above formula (A) further comprises condensing a 2,3,5-tri-O-protected-L-xylose derivative
10 followed by removal of the 2'-OH group by either halogenation or thiocarbonylation procedure. The 3'-OH group is then of epimerized to obtain the desired 2'-deoxy- β -L-nucleosides.

48. The process of claim 5 or 17 wherein the preparation of the compound of the above formula (A) containing a pyrimidine base further comprises condensing a 2,3,5-tri-O-
15 protected-L-ribose with a pyrimidine, followed by deoxygenation of 2'-OH by way of 2,2'-anhydronucleoside formation.

49. The process of claim 8 or 22 wherein the preparation of the compound of the above formula (A) containing a purine base further comprises condensing a 2,3,5-tri-O-
20 protected-L-xylose with a purine, followed by deoxygenating the 2'-OH by substitution with sulfur and reducing by desulfurization.

50. The process of claim 26 wherein, the preparation of the compound of the above formula (A) containing a purine base further comprises condensing a 2,3,5-tri-O-protected-L-
xylose with a purine, oxygenating the 2'-OH into a keto group and followed by removing the keto group by the Wolf-Kischner reduction or a similar modification.

51. The process of claim 26 wherein the preparation of the compound of the above formula (A) containing a pyrimidine base further comprises condensing a 2,3,5-tri-O-protected-L-
25 xylose with a pyrimidine, oxygenating the 2'-OH into a keto group and followed by removing the keto group by the Wolf-Kischner reduction or a similar modification..

52. The process of claim 3, 5 or 8 wherein the preparation of the compound of the above formula (A) comprises condensing a 2,3,5-tri-O-protected-L-arabinose with a purine or pyrimidine, followed by deoxygenating the 2'-OH via substitution of the OH or thiocarbonylation and subsequent reduction.

5 53. The process of claim 15 wherein the preparation further comprises synthesizing a crystalline 3,5-di-O-(p-methylbenzoyl)-2-deoxy- β -L-ribofuranosyl chloride through a novel process from L-arabinose.

54. The process of claim 32 wherein the preparation of the compound of the above formula (A) containing a purine base further comprises condensing a 2,3,5-tri-O-protected-D-
10 arabinose with a purine to obtain the corresponding β -D-nucleoside, then converting it into the desired β -L-arabino-nucleoside by inversion of the 4'-hydroxymethyl group.

55. The process of claim 32 wherein the preparation of the compound of the above formula (A) further comprises synthesizing the L-nucleoside from a natural β -D-nucleoside by successive anomerization and C-4' epimerization.